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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/776,252
Filing Date: February 02, 2001
Appellant(s): ELLINGTON, ANDREW

Travis M. Wohlers
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 28 February 2007 appealing from the Office action mailed 17 August 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,242,246	GOLD et al	6-2001
5,650,275	PITNER et al	7-1997
5,445,935	ROYER	8-1995
5,631,146	SZOSTAK et al	5-1997

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

New Matter

Claims 29-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 29 (from which all other claims depend) has been amended to recite "not by means of a separate quenching molecule". Appellant points to numerous passages in the specification that teach two aptamers having fluorescing moieties incorporated e.g. ATP-R-Ac13 has an acridine moiety replacing an adenosine at position 13 and DFL708 has a fluorescein molecule inserted between residues 7 and 8. While the two aptamers provided in the specification are not described as having a quenching molecule, the aptamers function to quench the signal. Furthermore, neither the cited passages nor the remaining text of the specification teaches what is encompassed by the negative limitation i.e. "not by means of a separate quenching molecule". For these reasons, the amendment is deemed new matter.

(10) Response to Argument

Appellant asserts that the aptamers described in the specification do not have quencher molecules incorporated into their sequences. Appellant asserts that a person of skill in the art would recognize a disclosure of the invention defined in the claims. Appellant asserts that the instant specification would "cry out" for a discussion of a quenching molecule if one were used and that the absence of such a discussion supports the negative recitation language of the claims.

Appellant's arguments have been noted, however as stated above, the specification does support an embodiment drawn to the exclusion of a quencher molecule. The specification defines a "signaling aptamer" as an aptamer with reporter molecules, the reporters providing a

differential signal upon aptamer/ligand interaction (page 14, lines 13-17). The specification further teaches working embodiments of two aptamers having fluorescing moieties incorporated into their sequence. The working embodiments illustrate a differential signal upon ligand/aptamer binding. However, it is maintained that the specification does not teach or define the exclusion of a "separate quenching molecule".

The specification further teaches that the reporter molecules encompass an unlimited variety of signaling molecules as follows (paragraph spanning pages 14-15):

> As used herein, the term "reporter molecule" shall include, but is not limited to, dyes that signal via fluorescence or dyes that signal via fluorescence or colorimetric intensity, anisotropy, polarization, lifetime, or changes in emission or excitation wavelengths. Reporter molecules may also include molecules that undergo changes in their electrochemical state such as in an oxidation-reduction reaction wherein the local environment of the electron carrier changes the reducing potential of the carried or may include enzymes that generate signals such as beta-galactosidase or luciferase.

The M.P.E.P § 2173.05(i) provides clear guidance regarding negative limitations:

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See In re Johnson, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also Ex parte Grasselli, 231 USPQ 393 (Bd. App. 1983), aff 'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

In the instant case, there is no positive recitation in the specification to support a claim drawn to the exclusion of quencher molecules. Furthermore, as noted above, the absence of a positive recitation is not basis for an exclusion. Hence, the absence of a quencher molecule teaching is not basis for a claim drawn to the exclusion of a quencher molecule.

It is the opinion of the examiner that had Appellant contemplated exclusion of quencher molecules from the scope of the invention, the specification would have contained some

suggestion of such an exclusion. However, the specification provides no such suggestion and as such does not set for the claimed subject matter is such a way as to reasonably convey to one of skill that appellant contemplated the claimed invention. Therefore, claims drawn to the exclusion of quencher molecules are deemed new matter.

Claim Rejections - 35 USC § 102

Claims 29-37 and 40-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Gold et al (U.S. Patent No. 6,242,246, filed 15 December 1997) as defined by Pitner et al (U.S. Patent No. 5,650,275, issued 22 July 1997).

Regarding Claim 29, Gold et al disclose a method of transducing a conformational change in a signaling aptamer, the method comprising the steps of providing a signaling aptamer and by means other than a quenching molecule (reporter molecule e.g. fluorescence label, luminescent label and near IR label, Column 15, lines 49-56) covalently coupled to an aptamer, i.e. the labeled aptamer is prepared by methods taught by Pitner, U.S. Patent No. 5650275, Column 15, lines 44-59) wherein unbound signaling aptamer is quenched relative to the signal when aptamer undergoes a conformational change upon binding its ligand (Column 13, lines 37-59 and Fig. 5). The method further comprises, containing the signaling aptamer with the ligand for binding and detecting signal produced by the reporter (Column 13, lines 37-59 and Fig. 5). Gold et al teach the labeled signaling aptamer is prepared by methods taught by Pitner, U.S. Patent No. 5,650,275 (Column 15, lines 44-59). Pitner defines the ligand labeling as covalent (Column 5, lines 7-9). Because Gold et al teaches the signaling aptamers are labeled using the method of Pitner and because Pitner teaches the aptamer is covalently coupled to the aptamer, Gold et al anticipates the covalently coupled aptamer-reporter as claimed.

Regarding Claim 30, Gold et al disclose the method further comprising quantifying the amount of label bound to the aptamer (Column 15, lines 57-65).

Regarding Claim 31, Gold et al disclose the method wherein the optical signal is fluorescence, anisotropy, polarization, lifetime or intensity (Column 15, lines 57-65).

Regarding Claim 32, Gold et al disclose the method wherein the covalent coupling occurs during synthesis (Column 15, lines 44-47)as defined by Pitner (Column 7, lines 11-19).

Regarding Claim 33, Gold et al disclose the method wherein the reporter is a dye (e.g. Column 15, lines 52-57).

Regarding Claim 34, Gold et al disclose the method wherein the dye is a fluorescent dye (e.g. Column 15, lines 52-57).

Regarding Claim 35, Gold et al disclose the method wherein the dye is attached according to the method of Pitner (Column 15, lines 44-47) and Pitner defines the dye attachment as insertion of a fluorescein at an internal position (Column 4, lines 32-43).

Regarding Claim 36, Gold et al disclose the method wherein the dye is acridine or fluorescein (e.g. Column 15, lines 52-57).

Regarding Claim 37, Gold et al disclose the method wherein the aptamer comprises modified or unmodified RNA or DNA (nucleic acid ligands, Column 5, lines 56-58) wherein nuclide acids are modified or unmodified RNA or DNA (Column 5, lines 23-43).

Regarding Claim 40, Gold et al disclose the method wherein the label is adjacent to a functional residue (i.e. "within the binding site of the target molecule, Column 16, lines 1-3) wherein the label is attached according to the method of Pitner (Column 15, lines 44-47) and Pitner defines the dye attachment as insertion of a fluorescein at an internal position (Column 4, lines 32-43).

Regarding Claim 42, Gold et al disclose the method wherein the aptamer is in solution i.e. the aptamer is crosslinked so that "interaction with target molecules will occur in solution" (Column 9, lines 8-12).

Regarding Claims 42-43, Gold et al disclose the method wherein the aptamer is immobilized on a chip (Column 13, lines 37-59 and Fig. 5).

(10) Response to Argument

Appellant asserts that Gold et al only teaches quenching molecules and therefore does not anticipate the instantly claimed method. The argument has been considered but is not found persuasive because as stated above, Gold et al specifically teaches numerous labels other than quenchers, the labels include fluorescent label, luminescent label and near IR label (Column 15, lines 49-56). While Gold et al illustrates the embodiment of conformational change using a fluorescent-quencher (F-Q) pair (Fig. 5), the reference clearly teaches a variety of other labels are used in the method (Column 15, lines 44-65). It is further noted that the labels of Gold et al are encompassed by the instantly claimed reporter molecules as defined in the instant specification (paragraph spanning pages 14-15).

Gold et al specifically teach the labels on the nucleic acid ligands (i.e. aptamers) "undergo a detectable change in fluorescence intensity, fluorescence polarization or fluorescence lifetime upon binding" (Column 15, lines 49-52) and provides a variety of labels useful in their method (Column 15, lines 52-62). Hence, Gold et al is clearly not limited to a quenching molecule as asserted.

Furthermore, Gold et al teaches the aptamers are produced using the method of Pitner et al (Column 15, lines 46-47) who also teaches labels include fluorescent label, luminescent label and near IR label (Column 4, line 32-43).

Claims 29-34, 36-37 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Royer (U.S. Patent No. 5,445,935, issued 29 August 1995).

It is noted that the Royer reference was used to reject the claims in the First Office Action on the Merits dated 29 March 2002. In the subsequent office action dated 26

November 2002, the rejection was "withdrawn as superfluous in view of the other two 102 rejections." Hence, the record does not show that the reference is not deemed prior art against the claims.

Regarding Claim 29, Royer discloses a method of transducing a conformational change in a signaling aptamer, the method comprising the steps of providing a signaling aptamer comprising a covalently bound reporter molecule that is not a quenching molecule (fluorescent label, Column 6, lines 34-47) wherein signal from the unbound aptamer is quenched relative to the aptamer bound to the target (Column 4, line 10-47), the method comprising the steps of contacting the aptamer with the ligand and detecting the optical signal produced by the aptamer upon ligand binding (Fig. 1).

Regarding Claim 30, Royer discloses the method further comprising quantifying the amount of label bound to the aptamer (Column 4, lines 45-48).

Regarding Claim 31, Royer discloses the method wherein the optical signal is fluorescence, anisotropy, polarization (Column 7, lines 40-51).

Regarding Claim 32, Royer discloses the method wherein the covalent coupling of the reporter occurs during synthesis (Column 6, lines 34-47).

Regarding Claim 33, Royer discloses the method wherein the reporter is a dye (e.g. fluorescein Column 6, lines 63-65).

Regarding Claim 34, Royer discloses the method wherein the dye is a fluorescent dye (e.g. fluorescein Column 6, lines 63-65).

Regarding Claim 36, Royer discloses the method wherein the dye is fluorescein (e.g. Column 6, lines 63-65).

Regarding Claim 37, Royer discloses the method wherein the aptamer comprises modified or unmodified RNA or DNA (Column 6, lines 48-50).

Regarding Claim 41, Royer discloses the method wherein the signaling aptamer is in solution (Column 9, lines 11-32).

(10) Response to Argument

Appellant asserts that Royer does not teach an optical signal is quenched by the aptamer's conformation. Appellant asserts that Royer measures a change in polarization of a labeled molecule wherein the change in polarization is a result in tumbling speed, not conformational change as instantly claimed. The argument has been considered but is not found persuasive. Royer et al specifically teaches detection of differential signal upon aptamer/ligand binding, the differential signal resulting from "complex formation" and "increase in size of the tumbling particle when .... complexed" (Column 4, lines 13-26) wherein the signal is fluorescence polarization or anisotropy (Column 4, lines 21-24 and Column 7, lines 39-42).

The instant claims are drawn to detecting an optical signal resulting from conformational change upon ligand/aptamer binding. The specification defines ""conformational changes" as "not limited to, changes in spatial arrangements including subtle changes in chemical environment without a concomitant spatial arrangement." (page 15, lines 17-20). The instant specification further defines "optical signals" as inclusive of fluorescence, colorimetric intensity, anisotropy, polarization (page 11, lines 20-21).

The complex formation and resulting increased size are encompassed by the conformational changes as defined by the instant specification. Furthermore, the optical signal detection of Royer is encompassed by that defined in the specification. Therefore, Royer anticipates the claimed invention as defined in the instant specification.

Claim Rejections - 35 USC § 103

Claims 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al (U.S. Patent No. 6,242,246, filed 15 December 1997) as defined by Pitner et al (U.S. Patent No.

5,650,275, issued 22 July 1997) in view of Szostak et al. (U.S. Patent No. 5,631,146, issued 20 May 1997).

Regarding Claim 38-39, Gold et al disclose a method of transducing a conformational change in a signaling aptamer, the method comprising the steps of providing a signaling aptamer (reporter molecule covalently coupled to an aptamer, i.e. the labeled aptamer is prepared by methods taught by Pitner, U.S. Patent No. 5650275, Column 15, lines 44-59) wherein unbound signaling aptamer is quenched relative to the signal when aptamer undergoes a conformational change upon binding its ligand (Column 13, lines 37-59 and Fig. 5). The method further comprises, containing the signaling aptamer with the ligand for binding and detecting signal produced by the reporter (Column 13, lines 37-59 and Fig. 5).

Gold et al teach their method is useful for detecting a variety of ligands for diagnosis of numerous important ligand-specific diseases (Column 7, line 48-Column 8, line 13) but they do not teach the aptamers are anti-adenosine RNA or DNA aptamer wherein the former is ATP-R-ACI3 and the latter is DFL7-8 and the ligand (target molecule) is adenosine.

However, Szostak et al teach anti-adenosine triphosphate and anti-adenosine DNA aptamers prepared by the same process (Column 4, line 56-column 6, line 9) and they further teach anti-adenosine aptamers are especially useful for ATP purification and in vivo quantification (Column 18, lines 31-42). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply anti-adenosine aptamers of Szostak et al to the target detection of Gold et al for the expected benefits of purification and in vivo quantification of an important target molecule as taught by Szostak et al (Column 18, lines 31-42).

(10) Response to Argument

Appellant asserts that Gold et al does not teach all the elements of Claim 29 and Szostak et al does not cure the deficiencies of Gold. The is not found persuasive for the reasons stated above regarding Gold.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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